

4. (Amended) The polypeptide of claim 3, wherein the variant is due to the translation of a single nucleotide polymorphism in a nucleic acid encoding said polypeptide.

5. (Amended) *B* The polypeptide of claim 1, wherein said polypeptide is a variant polypeptide comprising an amino acid sequence differing by one or more conservative substitutions from the amino acid sequence of SEQ ID NO:4.

Pursuant to 37 CFR 1.121(c)(1)(ii), a marked up version of the claims showing the changes made appears as Appendix A of this Amendment.

REMARKS

Upon entry of the present amendments, claims 1-5 and 40 will be pending in the application. Claims 1-5 have been amended. Support for the amendments appear in the original claims as filed. No new matter has been added by the amendments.

The pending claims have been objected to and/or rejected for various reasons. Each will be addressed individually below.

Formal Matters: Restriction under 35 U.S.C. §121 and 375 C.F.R. §1.142(a)

The Examiner states on page 2 of the Office Action that election of SEQ ID NO:4 in Paper No. 5 is not a species election, but rather is in response to a restriction requirement. Applicants traverse this representation and request that election of SEQ ID NO:4 be treated as a species election for the following reasons.

According to 35 U.S.C. §121, if two or more independent and distinct inventions are claimed in a single application, the Commissioner may require the application to be restricted to a single invention. According to 37 C.F.R. §§1.141(a) and 1.142(a), upon restriction, the Examiner shall require the applicant to elect that invention to which his claim shall be restricted.

However, MPEP 803.04, second and third paragraphs, states:

“Nevertheless, to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided sua sponte to partially waive the requirements of 37

CFR 1.141 et seq. and permit a reasonable number of such nucleotide sequences to be claimed in a single application. See Examination of Patent Applications Containing Nucleotide Sequences, 1192 O.G. 68 (November 19, 1996).

It has been determined that normally ten sequences constitute a reasonable number for examination purposes. Accordingly, in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction. In addition to the specifically selected sequences, those sequences which are patentably indistinct from the selected sequences will also be examined.

Furthermore, nucleotide sequences encoding the same protein are not considered to be independent and distinct inventions and will continue to be examined together."

MPEP 803.04 Restriction - Nucleotide Sequences

As stated in the specification on page 14, lines 31-35 (reproduced below in the section entitled "Rejection under 35 USC §112, first paragraph"), and as demonstrated in Exhibit A, FCTR1 and FCTR2 are splice variants of a common gene. The 132 aa polypeptide of SEQ ID NO:4 is 100% identical to the last 132 amino acids of SEQ ID NO:2. As reproduced above, MPEP 803.04 clearly states that nucleotide sequences encoding the same protein are not considered to be independent and distinct inventions and will continue to be examined together. Applicants respectfully request that SEQ ID NO:4 be examined as a species election.

Rejection under 35 U.S.C. §101 and §112

Claims 1-5 and 40 have been rejected under 35 USC §101 and §112 for allegedly lacking "credible, substantial or well-established utility". Applicants traverse and assert the present invention has a specific, substantial and credible utility.

Claim 1 from which the remaining claims depend, is directed to an isolated polypeptide having an amino acid sequence SEQ ID NO: 4. As the Examiner has noted, the polypeptide of the invention is generally referred to as 'FCTR_X' whereas the species that was elected is referred to specifically as 'FCTR2'. FCTR_X is related to various growth factors and growth factor families (see the Specification at page 2, lines 17-22) having particular uses, for example in one embodiment, as a therapeutic agent in promoting wound healing, neovascularization, tissue growth and similar tissue regeneration needs (see Specification at page 6, lines 7-11).

Consistent with the teachings in the specification, Applicants have discovered that the FCTR2 polypeptide, a splice variant of the 370 amino acid FCTR_X polypeptide sequence of the invention (such as SEQ ID NO. 2) or a functional fragment thereof, maintains FCTR_X-like

activities and physiological functions. For example, in one embodiment, the FCTR2 polypeptide has a functional similarity to various growth factors that are members of the platelet derived growth factor/vascular endothelial growth factor families (*See* specification at page 14, lines 36-39). For a comparison of FCTR1 and FCTR2, see Exhibit A.

The Examiner asserts that function cannot be predicted based solely on structural similarity to a known protein and cites various references as support. Applicants traverse. Applicants also note that specific function for FCTR2 is fully supported at least, *e.g.*, by Example 7 of the specification, as discussed further below.

Vukicevic, et al. (1996, PNAS USA 93:9021-9026) is cited for disclosing an example of one member of the TGF-family of proteins, OP-1, having metanephrogenesis activity while closely related TGF-family members, BMP-2 and TGF-1 did not have the same activity under identical conditions. Vukicevic does not teach the amino acid sequences, nucleic acid sequences and use of the FCTR_X proteins described in the present invention. Therefore, Vukicevic cannot be used to support the Examiner's lack of utility assertion.

Skolnick (2000, Trends in Biotech. 18:34-39, particularly Box 2) is cited for disclosing that the "protein structure by itself is insufficient to annotate a number of functional classes...and specific details of protein function" (Office Action, page 3).

The Examiner's reliance on Box 2 in Skolnick to provide evidence to support the rejection is deficient. Box 2 in Skolnick merely presents an example whereby proteins with similar structures can have different functions. Skolnick does not discuss the amino acid sequence, nucleic acid sequence and use of the FCTR_X proteins described in the present invention. Therefore, Skolnick cannot be used to support the Examiner's lack of utility assertion.

Doerks (1998, Trends in Genetics 14:248-250) is cited for disclosing overprediction of functionality as a result of lack of coincidence between structural similarity and functional similarity. Smith (1997, Nature Biotechnology 15:1222-1223) is cited for disclosing proteins having different functions but share structural similarity passed down through evolution. Brenner (1999, Trends in Genetics 15:132-133) is cited for disclosing the difficulty in inference of function from homology in view of the existence of only 1000 major gene superfamilies. Kopchick (US Patent 5,350,836) is cited for disclosing antagonists of vertebrate growth hormone that differ by a single amino acid from naturally occurring growth hormone. None of these

individual references describe the amino acid sequence, nucleic acid sequence and use of the FCTR_X proteins of the present invention. At best, these references merely represent generalities of the various techniques applied in predicting protein structure.

The Utility Examination Guidelines state that “when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the Examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion.” (Fed. Reg., Vol. 66. No. 4, January 5, 2001, p. 1096). If the Examiner has sufficient evidence to rebut such an assertion, and rejects the claims for lack of utility, then the burden shifts back to the Applicant to provide evidence supporting such a well-established utility. Applicants respectfully submit that the Examiner has not provided sufficient evidence or sound scientific reasoning in reliance on general references in the art to rebut the utility of the FCTR_X proteins claimed.

FCTR₂ nucleic acid can be used as a marker for certain cell types and disease states. In Example 7 of the specification (see page 116, line 30 to page 120, line 26), TaqMan expression data is shown for 30664188. The ClustalW in the attached Exhibit A aligns disclosed sequences to show that the TaqMan primer probe sets Ag33 and Ag168 (SEQ ID NOs:15-17 and 21-22, respectively) overlap with FCTR₂, whereas set Ag66 (SEQ ID NOs:18-20) does not.

Accordingly, the data presented in the first and third columns of Table 3 in Example 7 of the specification as filed apply to both FCTR₁ and FCTR₂. One skilled in the art would know that the difference between results from, *e.g.*, TaqMan data from primer probe set Ag33 versus primer probe set Ag66 may be attributable to the presence and absence, respectively, of FCTR₂. Applicants therefore traverse the Examiner’s statement on page 3 of the Office Action that “there is no actual experimental result of any kind to confirm any function associated with FCTR₂.

As stated above, Example 7 presents therein functional data for FCTR₂. The disclosed experimental results in Table 3 demonstrate that expression of FCTR₂ is increased in ovarian cancer cells, as compared to their normal tissue counterparts. Therefore, FCTR₂ has a utility as a marker for ovarian cancer disease states.

Furthermore, applicants have generated additional TaqMan data for FCTR2, which is presented in the attached Exhibit B. The FCTR2 TaqMan data shows that FCTR2 would serve as a useful marker for ovarian cancer cells, as well as for clear cell type kidney cancer cells, stomach cancer cells, and breast cancer cells. Accordingly, applicants assert that FCTR2 has a specific, substantial, and credible utility as a marker for various cancer states. For these and the above reasons, Applicants request withdrawal of this rejection.

Claims 1-5 and 40 are also rejected under 35 USC §112, first paragraph for alleging that since the invention is not supported by either a substantial or credible utility, one skilled in the art would not know how to use the claimed invention.

Applicants traverse. For the reasons set forth above, Applicants submit that the claimed invention satisfies the utility requirements under 35 USC §101. Therefore, these rejections are now moot as they apply to pending claims 1-5 and 40 and should be withdrawn.

Rejection under 35 USC §112, first paragraph

Claims 1-5 and 40 have been rejected under 35 USC §112, first paragraph, for allegedly lacking enablement for the scope of the claims that encompass no more than 15% difference in amino acid sequence to that of SEQ ID NO. 4, fragments and variants thereof and conservative substitutions thereof.

Claims 1-5 have been amended to delete references to variants having no more than 15% difference in amino acid sequence. Claim 40 depends from claim 1 and incorporates these changes by reference. The rejection is now moot.

The Examiner also asserts that the specification does not teach how to make and use FCTR2 variants or fragments. Applicants traverse and direct the Examiner's attention to various sections in the specification teaching how to make and use the polypeptide claimed. The amino acid sequence of SEQ ID NO: 4 or FCTR2 (and also referred to as "30664188.0.331 protein") is a variant of FCTR1. More specifically, FCTR2 is described in the specification, at page 14, lines 32-35:

[t]he 132 amino acids of the clone 30664188.0.331 protein are 100% identical to the carboxy-terminal region of the protein sequence of 30664188.0.99. Thus, the

nucleic acids of clones 30664188.0.99 and 30664188.0.331 are therefore related as splice variants of a common gene.

Accordingly, one of skill in the art would appreciate the significance in the regions of overlap or identity of these protein sequences, how to make the claimed protein and how to predict amino acid substitutions in the claimed protein following the Examples of cloning, expression, purification, and use of the FCTR1 polypeptide on pages 112-125 of the specification.

One of skill in the art would also recognize the conserved domains of various growth factors, as determined by BLASTN and BLASTP analysis as well as other publicly accessible sequence databases (*See* specification paragraph bridging page 11, line 44 to page 12, lines 11-20) within the overlapping regions of SEQ ID NO: 4 can be expected to function in the manner of similar growth factor protein domains found in SEQ ID NO:2. As such, diseases and conditions involving altered or aberrant function of members of specific growth factors, readily identifiable by the skilled artisan, could be analyzed using the nucleotide sequence of SEQ ID NO: 4 comprising the disclosed mature sequences of the present invention, variants or fragments thereof.

The Utility Guidelines state "when a class of proteins is defined such that the members share a specific, substantial and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein". Applicants have disclosed at least one practical utility for FCTR_X from which FCTR2 is a variant which maintains a specific, substantial and credible utility.

The function and structure of a known variant or reference protein such as FCTR1 gives the skilled artisan a clue to the function of the new variant, *i.e.*, FCTR2, especially if a particular sequence or domain was added or removed from the reference protein. (Federal Register, Vol. 66, No. 4, p. 1095 and 1096)

Accordingly, one skilled in the art following the specification would recognize that the disclosed variant, FCTR2, having 132 amino acids that are identical to the carboxy-terminal region of FCTR1 and variants thereof is made and used as taught in the present invention.

Applicants have attached herewith data (Exhibit C) that further supports the utility and enablement of the claimed polypeptide. As described in the specification at page 124, Example 13 "Purification of Intact and Cleaved Products of the 30664188.m99 Protein", a p35 FCTRX protein derived from the intact full length protein has growth promoting activities (See specification at page 121, Example 9) and inhibition of tumor growth (specification at page 122, Example 10). This fragment is the carboxy-terminal fragment of the full-length protein called p35 (See specification at page 123, Example 12, lines 25-28).

Applicants' further characterization of the p35 fragment and its biochemical properties has verified that the p35 protein fragment is a biologically active, cleaved product and is encompassed within SEQ ID NO: 4. Figure 14 in Exhibit A shows an SDS-PAGE analysis of a FCTRX polypeptide. Panel B shows a Coomassie stained FCTRX protein from ppCEP4/Sec-PDGF D transfected HEK 293 cells cultured in the presence of different culture media. Under serum-free conditions a 49kD gene product (p49) under reducing conditions was obtained. A polypeptide species with an apparent molecular weight of about 84 kDa, corresponding to a dimeric p85 species of p49, was seen under non-reducing conditions (Panel B, lane 1). Under serum-containing conditioned medium and nonreducing conditions, a species with an apparent molecular weight of about 36 kDa (p35) was observed (Panel B, lane 3). Under reducing conditions, p35 was found to yield three bands with apparent molecular weights of approximately 20, 14 and 6 kDa (Panel B, lane 4). Amino terminal sequence analysis of the p35 fragment demonstrated proteolytic cleavage after R247 or R249 (Figure 15).

Figure 15 in Exhibit C represents fragments obtained from p35 and identified by N-terminal sequencing. In each panel, the upper sequence in black is the predicted sequence from the clone, and the lower sequence in gray is the sequence provided by N-terminal sequencing. The diagonal shadings represent two fragments of p35. Horizontal shading represents the V5 epitope and vertical shading represents the 6His tag, both of which originate from vector pCEP4/Sec-30664188. In Panel A, two sequences were identified, one beginning with GlyArg (shown with these residues underlined), and the second beginning with the third residue, Ser.

These results indicate that the FCTRX protein of the present invention is secreted as the holoprotein (p85), which is processed in the culture medium to provide the C-terminal fragment

(p35). As noted above, the p35 form is encompassed within the presently claimed polypeptide, FCTR2. Thus, the structure, function, biological activity, and utility of the FCTR2 (SEQ ID NO: 4) protein has been identified and taught in the specification and the Examiner's rejection must be withdrawn. This rejection is now moot and should be withdrawn.

The Examiner has also rejected claim 3 and 4 under 35 USC §112, first paragraph for allegedly lacking adequate description in the allelic variants of SEQ ID NO: 4 and variants thereof. Applicants traverse.

Determining allelic variation and degeneracy of a nucleotide sequence and the proteins encoded thereby is known in the art. A patent need not teach what is well known in the art. Hybritech Inc. v. Monoclonal Antibodies, 231 USPQ 81, 1384 (Fed. Cir. 1986). Accordingly, one of skill in the art could readily produce allelic variants of the FCTR2 protein as claimed and following the art and teachings in the specification at page 25 line 19 - page 26, line 12. Additional disclosure of contemplated FCTR2 variants appear, *e.g.*, in sections entitled "FCTR2 Variants" and "Conservative Mutations" in the specification at page 25, line 19, to page 30, line 19.

For the foregoing reasons set forth above, Applicants submit that the claimed invention has specific and substantial or well established utility and teaches one of skill in the art how to make and use the claimed invention. This rejection is now moot and should be withdrawn.

Rejection under 35 USC §112, second paragraph

The Examiner has rejected claim 4 as being indefinite for the recitation "wherein the variant is the translation of". The rejection is now moot in view of the claim amendments presented herein and should be withdrawn.

CONCLUSION

It is submitted that the application is in condition for allowance, and such action is respectfully requested. A petition for extension of time is enclosed with this response. With this petition, this response is due on or before June 5, 2002.

Applicants: Shimkets *et al.*
U.S.S.N. 09/662,783

Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below. The Commissioner is authorized to charge any additional fees that may be due, or to credit any overpayment, to the undersigned's account, Deposit Account No. 50-0311, Ref. No. 15966-577.

Respectfully submitted,

Dated: June 5, 2002


Ivor R. Elrifi, Reg. No. 39,529

Attorneys for Applicants
c/o MINTZ, LEVIN, COHN, FERRIS,
GLOVSKY and POPEO, P.C.
One Financial Center
Boston, Massachusetts 02111
Tel: (617) 542-6000
Fax: (617) 542-2241

Appendix A.

Version marked to show changes made

Please amend the claims as follows:

1. (Amended) An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

- a) [an] amino acid sequence [selected from the group consisting of SEQ ID NO:2 and] SEQ ID NO:4;
 - b) a mature form of amino acid sequence SEQ ID NO:4 [a variant of an amino acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4, in which one or more of the amino acids specified in the chosen sequence is changed to a different amino acid, provided that no more than 15% of the amino acid residues in the amino acid sequence of said variant are changed];
 - c) [a mature form of an amino acid sequence chosen from the group consisting of SEQ ID NO:2 and SEQ ID NO:4; and
 - d)] a variant of a mature form of an amino acid sequence [selected from the group consisting] of [SEQ ID NO:2 and] SEQ ID NO:4[, in which one or more of the amino acids specified in the chosen sequence is changed to a different amino acid, provided that no more than 15% of the amino acid residues in the amino acid sequence of the variant of said mature form are changed]; and
- [e)] d) a fragment of the [an] amino acid sequence described in a) to c) [d)].

2. (Amended) The polypeptide of claim 1, wherein said polypeptide is a FCTR2 fragment of a FCTR_X polypeptide.

3. (Amended) The polypeptide of claim 1, wherein said polypeptide is a naturally occurring allelic variant of [SEQ ID NO:2 or] SEQ ID NO:4.

4. (Amended) The polypeptide of claim 3, wherein the variant is due to the translation of a single nucleotide polymorphism in a nucleic acid encoding said polypeptide.

5. (Amended) The polypeptide of claim 1, wherein said polypeptide is a variant polypeptide comprising an amino acid sequence differing by one or more conservative substitutions from the amino acid sequence of [SEQ ID NO:2 or] SEQ ID NO:4.



Exhibit A
ClustalW Alignment of FCTR1 and FCTR2

FCTR1 FCTR2	10 20 30 40 50

	CTAAAAAAATATGTTCTCTACAACACCAAGGCTCATTAAAATATTTAAAT
	50
FCTR1 FCTR2	----- 1

	60 70 80 90 100

	ATTAATATACATTCTTCTGTCAAGAAATACATAAAACTTATTATATCAG
	100
FCTR1 FCTR2	----- 1

FCTR1 FCTR2	110 120 130 140 150

	CGCAGGGCGGGCGGGCGTCGGTCCCGGGAGCAGAACCCGGCTTTCTTG
	150
FCTR1p	----- 1

FCTR1 FCTR2 FCTR1p	160 170 180 190 200

	GAGCGACGCTGTCTCTAGTCGCTGATCCCAAATGCACCGGCTCATTTG
	200
FCTR1p	MetHisArgLeuIlePheV
FCTR1 FCTR2 FCTR1p	210 220 230 240 250

	TCTACACTCTAACATGCGCAAACTTTGAGCTGTCGGACACTCTGCA
	250
FCTR2	----- 1

FCTR1p	AlTyrThrLeuIleCysAlaAsnPheCysSerCysArgAspThrSerAla
FCTR1 FCTR2 FCTR1p	260 270 280 290 300

	ACCCCGAGAGCGATCCATCAAAGCTTGCGAACGCCAACCTCAGGCG
	300
FCTR2	----- 1

FCTR1p	ThrProGlnSerAlaSerIleLysAlaLeuArgAsnAlaAsnLeuArgAr
FCTR1 FCTR2 FCTR1p	310 320 330 340 350

	AGATGAGAGCAATCACCTCACAGACTGTACCGAAGAGATGAGACCATCC
	350
FCTR2	-----AGAGGCTCTCA 11

FCTR1p	GAspGluSerAsnHisLeuThrAspLeuTyrArgArgAspGluThrIleG
FCTR1 FCTR2 FCTR1p	360 370 380 390 400

	AGGTGAA-AGGAAACGGCTACGTGCAGAGTCTAGATTCCC
	GAACAGCT 398
FCTR2	-----GAAGAG-T 49

FCTR1p	LnValLy--sGlyAsnGlyTyrValGlnSerProArgPheProAsnSerT
FCTR1 FCTR2 FCTR1p	410 420 430 440 450

	ACCCCAGGAACCTGCTCCTGACATGGCGGCTTCACTCTCAGGAGAATACA
	448
FCTR2	-----GAACCTGCTCCTGACATGGCGGCTTCACTCTCAGGAGAATACA 92

FCTR1p	PyrroArgAsnLeuLeuLeuThrTrpArgLeuHisSerGlnGluAsnThr

Exhibit A (cont.)

	460	470	480	490	500	
FCTR1	CGGATACAGCTAGTGTGACAATCAGTTGGATTAGAGGAAGCAGAAAA					498
FCTR2	CGGATACAGCTAGTGTGACAATCAGTTGGATTAGAGGAAGCAGAAAA					142
FCTR1p	ArgIleGlnLeuValPheAspAsnGlnPheGlyLeuGluGluAlaGluAs					
	510	520	530	540	550	
FCTR1	TGATATCTGTAGGTATGATTTGTGAAAGTTGAAGATATATCCGAAACCA					548
FCTR2	TGATATCTGTAGGTATGATTTGTGAAAGTTGAAGATATATCCGAAACCA					192
FCTR1p	nAspIleCysArgTyrAspPheValGluValGluAspIleSerGluThrs					
	560	570	580	590	600	
FCTR1	GTACCATTATTAGAGGACGATGGTGTGGACACAAGGAAGTTCCCTCCAAGG					598
FCTR2	GTACCATTATTAGAGGACGATGGTGTGGACACAAGGAAGTTCCCTCCAAGG					242
FCTR1p	erThrIleIleArgGlyArgTrpCysGlyHisLysGluValProProArg					
	610	620	630	640	650	
Ag66	-----	-----	-----	-----	-----	
ATA	-----	-----	-----	-----	-----	
FCTR1	ATAAAATCAAGAACGAAACCAATTAAAATCACATTCAAGTCCGATGACTA					648
FCTR2	ATAAAATCAAGAACGAAACCAATTAAAATCACATTCAAGTCCGATGACTA					292
FCTR1p	IleLysSerArgThrAsnGlnIleLysIleThrPheLysSerAspAspTy					
	660	670	680	690	700	
Ag66 (F)	-----	-----	-----	-----	-----	
CTTTGTGGCTAACACCTGGATT						
FCTR1	CTTTGTGGCTAACACCTGGATTCAAGATTATTCTTTGCTGGAAAGATT					698
FCTR2	CTTTGTGGCTAACACCTGGATTCAAGATTATTCTTTGCTGGAAAGATT					342
FCTR1p	hrPeValAlaLysProGlyPheLysIleTyrTyrSerLeuLeuGluAspP					
	710	720	730	740	750	
FCTR1	TCCAACCCGCAGCAGCTTCAGAGACCAACTGGGAATCTGTACAAGCTCT					748
FCTR2	TCCAACCCGCAGCAGCTTCAGAGACCAACTGGGAATCTGTACAAGCTCT					392
FCTR1p	heGlnProAlaAlaAlaSerGluThrAsnTrpGluSerValThrSerSer					
	760	770	780	790	800	
FCTR1	ATTTCAGGGGTATCCTATAACTCTCATCAGTAACGGATCCCACACTCTGAT					798
FCTR2	ATTTCAGGGGTATCCTATAACTCTCATCAGTAACGGATCCCACACTCTGAT					442
FCTR1p	IleSerGlyValSerTyrAsnSerProSerValThrAspPrcThrLeuI					
	810	820	830	840	850	
FCTR1	TGCGGATGCTCTGGACAAAAAAATTGCGAGATTGATAACAGTGGAAAGATC					848
FCTR2	TGCGGATGCTCTGGACAAAAAAATTGCGAGATTGATAACAGTGGAAAGATC					492
FCTR1p	eAlaAspAlaLeuAspLysLysIleAlaGluPheAspThrValGluAspL					

Exhibit A (cont.)

860 870 880 890 900

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|

FCTR1 **TGCTCAAGTACTCAATCCAGAGTCATGGCAAGAAGATCTTGAGAATATG** 898
FCTR2 **TGCTCAAGTACTCAATCCAGAGTCATGGCAAGAAGATCTTGAGAATATG** 542
FCTR1p euLeuLysTyrPheAsnProGluSerTrpGlnGluAspLeuGluAsnMet
FCTR2p Met

910 920 930 940 950

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|

Ag33 (R) -----
CGGTATCGAGGCAGGTCTATA

FCTR1 **TATCTGGACACCCCTCGGTATCGAGGCAGGTCTACCATGACCGGAAGTC** 948
FCTR2 **TATCTGGACACCCCTCGGTATCGAGGCAGGTCTACCATGACCGGAAGTC** 592
FCTR1p TyrLeuAspThrProArgTyrArgGlyArgSerTyrHisAspArgLysSe
FCTR2p TyrLeuAspThrProArgTyrArgGlyArgSerTyrHisAspArgLysSe

960 970 980 990 1000

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|

-----Ag33 (F)
CTCAATGATGATGCCAAGCG

FCTR1 **AAAAGTTGACCTGGATAGGCTCAATGATGATGCCAAGCGTTACAGTTGCA** 998
FCTR2 **AAAAGTTGACCTGGATAGGCTCAATGATGATGCCAAGCGTTACAGTTGCA** 642
FCTR1p rLysValAspLeuAspArgLeuAsnAspAspAlaLysArgTyrSerCysT
FCTR2p rLysValAspLeuAspArgLeuAsnAspAspAlaLysArgTyrSerCysT

1010 1020 1030 1040 1050

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|

FCTR1 **CTCCCAGGAATTACTCGGTCAATATAAGAGAAAGAGCTGAAGTTGGCCAAT** 1048
FCTR2 **CTCCCAGGAATTACTCGGTCAATATAAGAGAAAGAGCTGAAGTTGGCCAAT** 692
FCTR1p hrProArgAsnTyrSerValAsnIleArgGluGluLeuLysLeuAlaAsn
FCTR2p hrProArgAsnTyrSerValAsnIleArgGluGluLeuLysLeuAlaAsn

1060 1070 1080 1090 1100

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|

Ag168 (R) -----
TCCACGTTGCCTCTCGT

FCTR1 **GTGGTCTTCTTCCACGTTGCCTCTCGTCAGCGCTGTGGAGGAAATTG** 1098
FCTR2 **GTGGTCTTCTTCCACGTTGCCTCTCGTCAGCGCTGTGGAGGAAATTG** 742
FCTR1p ValValPhePheProArgCysLeuLeuValGlnArgCysGlyGlyAsnCy
FCTR2p ValValPhePheProArgCysLeuLeuValGlnArgCysGlyGlyAsnCy

1110 1120 1130 1140 1150

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|

-----Ag168 (R)
ACTGGAGGTCTGCACATGC

FCTR1 **TGGCTGTGGAACTGTCAACTGGAGGTCTGCACATGCAATTCAAGGGAAAA** 1148
FCTR2 **TGGCTGTGGAACTGTCAACTGGAGGTCTGCACATGCAATTCAAGGGAAAA** 792
FCTR1p sGlyCysGlyThrValAsnTrpArgSerCysThrCysAsnSerGlyLysT
FCTR2p sGlyCysGlyThrValAsnTrpArgSerCysThrCysAsnSerGlyLysT

Exhibit A (cont.)

	1160	1170	1180	1190	1200
FCTR1	CCGTGAAAAAGTATCATGAGGTATTACAGTTGAGCCTGGCCACATCAAG				1198
FCTR2	CCGTGAAAAAGTATCATGAGGTATTACAGTTGAGCCTGGCCACATCAAG				842
FCTR1p	hrValLysLysTyrHisGluValLeuGlnPheGluProGlyHisIleLys				
FCTR2p	hrValLysLysTyrHisGluValLeuGlnPheGluProGlyHisIleLys				
	1210	1220	1230	1240	1250
FCTR1	AGGAGGGGTAGAGCTAACGACCATGGCTTAGTTGACATCCAGTTGGATCA				1248
FCTR2	AGGAGGGGTAGAGCTAACGACCATGGCTTAGTTGACATCCAGTTGGATCA				892
FCTR1p	ArgArgGlyArgAlaLysThrMetAlaLeuValAspIleGlnLeuAspHi				
FCTR2p	ArgArgGlyArgAlaLysThrMetAlaLeuValAspIleGlnLeuAspHi				
	1260	1270	1280	1290	1300
FCTR1	CCATGAACGATGTGATTGTATCTGCAGCTAACGACCACTCGATAAGAGA				1298
FCTR2	CCATGAACGATGTGATTGTATCTGCAGCTAACGACCACTCGATAAGAGA				942
FCTR1p	sHisGluArgCySAspCysIleCysSerSerArgProProArg				
FCTR2p	sHisGluARgCysAspCysIleCysSerSerArgProProArg				
	1310	1320	1330	1340	1350
FCTR1	ATGTGCACATCCTTACATTAAGCCTGAAAGAACCTTTAGTTAAGGAGGG				1348
FCTR2	ATGTGCACATCCTTACATTAAGCCTGAAAGAACCTTTAGTTAAGGAGGG				992
	1360	1370	1380	1390	1400
FCTR1	TGAGATAAGAGACCCCTTCTACCAGCAACCAAACCTACTACTAGCCTG				1398
FCTR2	TGAGATAAGAGACCCCTTCTACCAGCAACCAAACCTACTACTAGCCTG				1042
	1410	1420	1430	1440	1450
FCTR1	CAATGCAATGAACACAAGTGGTTGCTGAGTCTCAGCCTGCTTGTTAAT				1448
FCTR2	CAATGCAATGAACACAAGTGGTTGCTGAGTCTCAGCCTGCTTGTTAAT				1092
	1460	1470	1480	1490	1500
FCTR1	GCCATGGCAAGTAGAAAGGTATATCATCAACTTCTATACCTAACGAAATATA				1498
FCTR2	GCCATGGCAAGTAGAAAGGTATATCATCAACTTCTATACCTAACGAAATATA				1142
	1510	1520	1530	1540	1550
FCTR1	GGATTGCATTTAATAATAGTGGTTGAGGTTATATATGCACAAACACACAC				1548
FCTR2	GGATTGCATTTAATAATAGTGGTTGAGGTTATATATGCACAAACACACAC				1192
	1560	1570	1580	1590	1600
FCTR1	AGAAAATATATTGATGCTATGTTGATATAGATCAAATGTTTTTTGGTA				1598
FCTR2	AGAAAATATATTGATGCTATGTTGATATAGATCAAATGTTTTTTGGTA				1242
	1610	1620	1630	1640	1650
FCTR1	TATATAACCAAGGTACACCAGAGCTTACATATGTTGAGTTAGACTCTTAA				1648
FCTR2	TATATAACCAAGGTACACCAGAGCTTACATATGTTGAGTTAGACTCTTAA				1292

Exhibit A (cont.)

	1660	1670	1680	1690	1700	
FCTR1	AATCCTTGCCAAAATAAGGGATGGTCAAATATGAAACATGTCTTTAG					1698
FCTR2	AATCCTTGCCAAAATAAGGGATGGTCAAATATGAAACATGTCTTTAG					1342
	1710	1720	1730	1740	1750	
FCTR1	AAAATTAGGAGATAAAATTATTTAAATTGAAACACAAAACAATT					1748
FCTR2	AAAATTAGGAGATAAAATTATTTAAATTGAAACACAAAACAATT					1392
	1760	1770	1780	1790	1800	
FCTR1	TGAATCTTGCTCTCTAAAGAAAGCATCTTGTATATTAAAAATCAAAAGA					1798
FCTR2	TGAATCTTGCTCTCTAAAGAAAGCATCTTGTATATTAAAAATCAAAAGA					1442
	1810	1820	1830	1840	1850	
FCTR1	TGAGGCTTCCTTACATATACATCTTAGTTG-----					1828
FCTR2	TGAGGCTTCCTTACATATACATCTTAGTTGATTATTAAAAAGGAAAAAT					1492
	1860	1870	1880	1890	1900	
FCTR1	-----					1828
FCTR2	ATGGTTCCAGAGAAAAGGCCAACCTAACGATTTTCCATGAGAAGC					1542
	1910	1920	1930	1940		
FCTR1	-----					1828
FCTR2	ACTGCATACTTACCTATGTGGACTATAAACCTGTCTCCAAAC					1587

Legend for Exhibit A:

- Row1: FCTR1 (SEQ ID NO:1)
- Row2: FCTR2 (SEQ ID NO:3)
- Row3: FCTR1p (SEQ ID NO:2)
- Row4: FCTR2p (SEQ ID NO:4)



Exhibit B

TaqMan Panels: Ag 66 primer set - FCTR1 only.

Ag33 and Ag168 primer set - FCTR1 and FCTR2 combined.

Table 1

Panel #1 Ag33 TaqMan Primers		
Tissue Name	Rel. Expr., % tm193f	Rel. Expr., % tm231t
Endothelial cells	1.2	1.7
Endothelial cells (treated)	1.5	2.8
Pancreas	28.7	36.3
Pancreatic ca. CAPAN 2	0.5	1
Adipose	30.6	10.4
Adrenal gland	100	100
Thyroid	8.2	20.4
Salavary gland	6.7	6.5
Pituitary gland	4	5.8
Brain (fetal)	2.3	2.2
Brain (whole)	2.7	3.5
Brain (amygdala)	0.9	1.3
Brain (cerebellum)	1	1.3
Brain (hippocampus)	1.9	3.3
Brain (substantia nigra)	0	2
Brain (thalamus)	0.2	0.4
Brain (hypothalamus)	37.1	42.9
Spinal cord	2.8	4.6
CNS ca. (glio/astro) U87-MG	0	0
CNS ca. (glio/astro) U-118-MG	0	0
CNS ca. (astro) SW1783	1.5	1.9
CNS ca.* (neuro; met) SK-N-AS	1	2
CNS ca. (astro) SF-539	0.1	0.3
CNS ca. (astro) SNB-75	5.3	5.3
CNS ca. (glio) SNB-19	3.6	3.8
CNS ca. (glio) U251	1.7	2.8
CNS ca. (glio) SF-295	53.6	82.4
Heart	13.6	14.7
Skeletal muscle	1	1.3
Bone marrow	0.7	1.2
Thymus	2.8	6
Spleen	1.8	2.2
Lymph node	3.7	5.8
Colon (ascending)	3.6	2.1

Stomach	26.1	24.7
Small intestine	5.1	6
Colon ca. SW480	0	0
Colon ca.* (SW480 met)SW620	0	0
Colon ca. HT29	0	0
Colon ca. HCT-116	0	0
Colon ca. CaCo-2	0	0
Colon ca. HCT-15	0	0
Colon ca. HCC-2998	0	0
Gastric ca.* (liver met) NCI-N87	0	0
Bladder	13.2	2.9
Trachea	15.8	24.5
Kidney	4.1	5.4
Kidney (fetal)	10.1	14.2
Renal ca. 786-0	0	0
Renal ca. A498	0.5	0.8
Renal ca. RXF 393	0	0
Renal ca. ACHN	0.4	0.7
Renal ca. UO-31	0	0.1
Renal ca. TK-10	0.6	1.5
Liver	4.4	5.4
Liver (fetal)	1.1	1.6
Liver ca. (hepatoblast) HepG2	0	0
Lung	1.3	0.3
Lung (fetal)	1.6	2.7
Lung ca. (small cell) LX-1	0	0
Lung ca. (small cell) NCI-H69	0.4	0.6
Lung ca. (s.cell var.) SHP-77	0	0
Lung ca. (large cell)NCI-H460	0	0
Lung ca. (non-sm. cell) A549	6.1	7
Lung ca. (non-s.cell) NCI-H23	0.1	0.2
Lung ca (non-s.cell) HOP-62	2	2.8
Lung ca. (non-s.cl) NCI-H522	0	0
Lung ca. (squam.) SW 900	11.2	11.5
Lung ca. (squam.) NCI-H596	4.1	5
Mammary gland	31.4	32.8
Breast ca.* (pl. effusion) MCF-7	0	0
Breast ca.* (pl.ef) MDA-MB-231	0	0
Breast ca.* (pl. effusion) T47D	0.1	0
Breast ca. BT-549	0	0
Breast ca. MDA-N	0	0
Ovary	11	9.6
Ovarian ca. OVCAR-3	0.2	0.8
Ovarian ca. OVCAR-4	0.2	0.3
Ovarian ca. OVCAR-5	78.5	81.8

Ovarian ca.	OVCAR-8	1.5	2.1
Ovarian ca.	IGROV-1	2	3
Ovarian ca.* (ascites)	SK-OV-3	0	0.1
Uterus		4.9	8.3
Placenta		5.8	7.3
Prostate		4	5.6
Prostate ca.* (bone met)	PC-3	0	0
Testis		21.5	20.9
Melanoma	Hs688(A).T	0.4	0.9
Melanoma* (met)	Hs688(B).T	0.5	0.9
Melanoma	UACC-62	0.1	0.2
Melanoma	M14	0.2	0.7
Melanoma	LOX IMVI	1	1.6
Melanoma* (met)	SK-MEL-5	0.5	1.5
Melanoma	SK-MEL-28	4.4	6

Table 1.2

Panel #1.2 Ag33 TaqMan Primers		
Tissue Name	Rel. Expr., % 1.2tm1460t_ag33	Rel. Expr., % 1.2tm1461t_ag33
Endothelial cells	2.2	0.4
Endothelial cells (treated)	4.6	1.7
Pancreas	6.2	2.6
Pancreatic ca.	CAPAN 2	0.2
Adrenal Gland (new lot*)	100	66
Thyroid	3.8	1
Salavary gland	9.8	9.3
Pituitary gland	10.5	9.7
Brain (fetal)	0.5	0
Brain (whole)	1.3	0
Brain (amygdala)	0.8	0
Brain (cerebellum)	0.2	0
Brain (hippocampus)	1.8	0
Brain (thalamus)	0.2	0
Cerebral Cortex	3.3	0
Spinal cord	3	1
CNS ca. (glio/astro)	U87-MG	0
CNS ca. (glio/astro)	U-118-MG	0
CNS ca. (astro)	SW1783	1.5
CNS ca.* (neuro; met)	SK-N-AS	1.6
CNS ca. (astro)	SF-539	0
CNS ca. (astro)	SNB-75	2.4
CNS ca. (glio)	SNB-19	2.1
CNS ca. (glio)	U251	2.2

CNS ca. (glio)	SF-295	39.8	29.9
Heart		30.8	26.2
Skeletal Muscle (new lot*)		2.6	0.7
Bone marrow		0.2	0
Thymus		0.5	0
Spleen		0.7	0
Lymph node		2.8	0.5
Colorectal		1.7	0
Stomach		21.5	16.3
Small intestine		5.2	1.7
Colon ca.	SW480	0	0
Colon ca.* (SW480 met) SW620		0	0
Colon ca.	HT29	0	0
Colon ca.	HCT-116	0	0
Colon ca.	CaCo-2	0	0
83219 CC Well to Mod Diff (ODO3866)		0.7	0
Colon ca.	HCC-2998	0	0
Gastric ca.* (liver met) NCI-N87		0	0
Bladder		31.9	25.7
Trachea		1.9	0.2
Kidney		7.5	4.4
Kidney (fetal)		12.9	10.3
Renal ca.	786-0	0	0
Renal ca.	A498	0.6	0
Renal ca.	RXF 393	0	0
Renal ca.	ACHN	0.4	0
Renal ca.	UO-31	0	0
Renal ca.	TK-10	0.3	0
Liver		1.8	0.2
Liver (fetal)		0.9	0
Liver ca. (hepatoblast) HepG2		0	0
Lung		0.5	0
Lung (fetal)		0.5	0
Lung ca. (small cell)	LX-1	0	0
Lung ca. (small cell)	NCI-H69	0.5	0
Lung ca. (s.cell var.)	SHP-77	1	0
Lung ca. (large cell)	NCI-H460	0	0
Lung ca. (non-sm. cell)	A549	8	8.7
Lung ca. (non-s.cell)	NCI-H23	0	0
Lung ca (non-s.cell)	HOP-62	4.9	0
Lung ca. (non-s.cl)	NCI-H522	0	0
Lung ca. (squam.)	SW 900	9.2	8.1
Lung ca. (squam.)	NCI-H596	4.3	1
Mammary gland		11	8.2
Breast ca.* (pl. effusion)	MCF-7	0	0

Breast ca.* (pl.ef) MDA-MB-231	0	0
Breast ca.* (pl. effusion) T47D	0	0
Breast ca. BT-549	1.2	0
Breast ca. MDA-N	0	0
Ovary	10.1	4.9
Ovarian ca. OVCAR-3	0.3	0
Ovarian ca. OVCAR-4	0	0
Ovarian ca. OVCAR-5	57.8	47.6
Ovarian ca. OVCAR-8	1.3	0
Ovarian ca. IGROV-1	3.6	0.7
Ovarian ca.* (ascites) SK-OV-3	0	0
Uterus	4.8	2.2
Placenta	10.4	6.8
Prostate	4.3	2.5
Prostate ca.* (bone met)PC-3	4.4	0.7
Testis	2.3	0.3
Melanoma Hs688(A).T	0.2	0
Melanoma* (met) Hs688(B).T	0.2	0
Melanoma UACC-62	0.5	0
Melanoma M14	0.3	0
Melanoma LOX IMVI	0	0
Melanoma* (met) SK-MEL-5	1.2	100
Adipose	10.5	4.4

Table 2D

Panel 2D, Ag33 vs. Ag66 TaqMan Primers			
Tissue Name	Rel. Expr., % 2dtm3995t_ag33	Rel. Expr., % 2dtm3998f_ag66	Rel. Expr., % 2dtm4046f_ag66
Normal Colon GENPAK 061003	19.6	34	22
83219 CC Well to Mod Diff (ODO3866)	1.3	2.9	1.6
83220 CC NAT (ODO3866)	2.9	2	3.5
83221 CC Gr.2 rectosigmoid (ODO3868)	0.5	1.4	0.6
83222 CC NAT (ODO3868)	1.3	1.5	0.6
83235 CC Mod Diff (ODO3920)	1.6	3.2	2.3
83236 CC NAT (ODO3920)	4.7	5.3	3.5
83237 CC Gr.2 ascend colon (ODO3921)	6.3	8.2	8.2
83238 CC NAT (ODO3921)	4.2	4.2	3.3
83241 CC from Partial Hepatectomy (ODO4309)	2.7	2.6	3.6
83242 Liver NAT (ODO4309)	1.9	1.7	2.7
87472 Colon mets to lung (OD04451-01)	0.6	0.8	1
87473 Lung NAT (OD04451-02)	2.5	4.1	2.4
Normal Prostate Clontech A+ 6546-1	3.7	5.3	4.4
84140 Prostate Cancer (OD04410)	4.4	10	9.1
84141 Prostate NAT (OD04410)	8.5	8.8	10
87073 Prostate Cancer (OD04720-01)	14.4	12	17

87074 Prostate NAT (OD04720-02)	18.3	31	19
Normal Lung GENPAK 061010	11	6.3	9.1
83239 Lung Met to Muscle (ODO4286)	1.4	1.1	0.5
83240 Muscle NAT (ODO4286)	9.9	8.1	10
84136 Lung Malignant Cancer (OD03126)	9.2	12	8.8
84137 Lung NAT (OD03126)	3.5	3.5	3.7
84871 Lung Cancer (OD04404)	2.6	2.2	2.7
84872 Lung NAT (OD04404)	6.6	7.2	8.9
84875 Lung Cancer (OD04565)	1.8	3.2	2.5
84876 Lung NAT (OD04565)	0.8	2.2	3.2
85950 Lung Cancer (OD04237-01)	4.1	4.2	4.8
85970 Lung NAT (OD04237-02)	7.6	7.9	6.4
83255 Ocular Mel Met to Liver (ODO4310)	5.6	5.6	6.9
83256 Liver NAT (ODO4310)	2.2	1.8	1.3
84139 Melanoma Mets to Lung (OD04321)	0.5	0.6	0.5
84138 Lung NAT (OD04321)	1.8	1.6	1.7
Normal Kidney GENPAK 061008	18.7	17	20
83786 Kidney Ca, Nuclear grade 2 (OD04338)	11.6	11	15
83787 Kidney NAT (OD04338)	10.7	13	12
83788 Kidney Ca Nuclear grade 1/2 (OD04339)	16.5	20	17
83789 Kidney NAT (OD04339)	10.4	8.7	8.8
83790 Kidney Ca, Clear cell type (OD04340)	100	100	100
83791 Kidney NAT (OD04340)	10.7	9.6	12
83792 Kidney Ca, Nuclear grade 3 (OD04348)	4.7	6.9	4.5
83793 Kidney NAT (OD04348)	4.5	4.7	5.3
87474 Kidney Cancer (OD04622-01)	9.2	12	10
87475 Kidney NAT (OD04622-03)	1	0.8	1.2
85973 Kidney Cancer (OD04450-01)	10.2	9.5	5.5
85974 Kidney NAT (OD04450-03)	7.7	11	12
Kidney Cancer Clontech 8120607	2.3	0.9	0.9
Kidney NAT Clontech 8120608	1.3	0.9	0.9
Kidney Cancer Clontech 8120613	1.6	1	1
Kidney NAT Clontech 8120614	1	0.7	1
Kidney Cancer Clontech 9010320	10.1	11	11
Kidney NAT Clontech 9010321	2.4	1.5	2.1
Normal Uterus GENPAK 061018	6.2	7.8	9.5
Uterus Cancer GENPAK 064011	14	14	12
Normal Thyroid Clontech A+ 6570-1	16.6	15	16
Thyroid Cancer GENPAK 064010	6.2	5.8	7.5
Thyroid Cancer INVITROGEN A302152	7.3	6.2	5.2
Thyroid NAT INVITROGEN A302153	17	15	14
Normal Breast GENPAK 061019	50.7	36	39
84877 Breast Cancer (OD04566)	4.2	5.6	5.4
85975 Breast Cancer (OD04590-01)	13.6	17	18
85976 Breast Cancer Mets (OD04590-03)	21	20	22

87070 Breast Cancer Metastasis (OD04655-05)	4.6	4	4.7
GENPAK Breast Cancer 064006	4.4	6.2	6.3
Breast Cancer Res. Gen. 1024	17.9	17	19
Breast Cancer Clontech 9100266	8.5	8.8	9.8
Breast NAT Clontech 9100265	14.5	14	16
Breast Cancer INVITROGEN A209073	32.5	37	40
Breast NAT INVITROGEN A2090734	22.2	29	23
Normal Liver GENPAK 061009	0.9	1.2	1.1
Liver Cancer GENPAK 064003	1.8	1.9	1.8
Liver Cancer Research Genetics RNA 1025	1.5	0.6	0.8
Liver Cancer Research Genetics RNA 1026	1.3	0.4	0.9
Paired Liver Cancer Tissue Research Genetics RNA 6004-T	1.2	1.1	1.9
Paired Liver Tissue Research Genetics RNA 6004-N	1.1	1.4	2.2
Paired Liver Cancer Tissue Research Genetics RNA 6005-T	1	0.5	1
Paired Liver Tissue Research Genetics RNA 6005-N	0.2	0.6	0.4
Normal Bladder GENPAK 061001	66	86	68
Bladder Cancer Research Genetics RNA 1023	2	1.6	2
Bladder Cancer INVITROGEN A302173	6.6	8.1	9.5
87071 Bladder Cancer (OD04718-01)	1.3	1.6	1.8
87072 Bladder Normal Adjacent (OD04718-03)	12.4	14	11
Normal Ovary Res. Gen.	8.6	7.9	9.5
Ovarian Cancer GENPAK 064008	65.1	90	67
87492 Ovary Cancer (OD04768-07)	14.3	15	12
87493 Ovary NAT (OD04768-08)	5.3	8.3	9.3
Normal Stomach GENPAK 061017	20	25	20
Gastric Cancer Clontech 9060358	3.7	2.7	3.8
NAT Stomach Clontech 9060359	10.5	15	11
Gastric Cancer Clontech 9060395	7.6	8.1	7.6
NAT Stomach Clontech 9060394	10.4	8.5	10
Gastric Cancer Clontech 9060397	5.3	6	5.5
NAT Stomach Clontech 9060396	3.1	3.4	2.8
Gastric Cancer GENPAK 064005	5.7	8.3	7.3

Table 3D

Panel 3D, Ag33 vs. Ag66 TaqMan Primers			
Tissue Name	Rel. Expr., % 3Dtm3446t_ag33	Rel. Expr., % 3Dtm3447f_ag66	
94905_Daoy_Medulloblastoma/Cerebellum_sscDNA	0	0	
94906_TE671_Medulloblastom/Cerebellum_sscDNA	3.1	4.5	
94907_D283_Med_Medulloblastoma/Cerebellum_sscDNA	2.4	2.7	
94908_PFSK-1_Primitive Neuroectodermal/Cerebellum_sscDNA	0.9	0.8	
94909_XF-498_CNS_sscDNA	0.4	0.6	
94910_SNB-78_CNS/glioma_sscDNA	0	0	

94911 SF-268 CNS/glioblastoma sscDNA	0	0.2
94912 T98G Glioblastoma sscDNA	100	100
96776 SK-N-SH Neuroblastoma (metastasis) sscDNA	10.8	10.4
94913 SF-295 CNS/glioblastoma sscDNA	22.5	22.8
94914 Cerebellum sscDNA	1.3	1.2
96777 Cerebellum sscDNA	0.6	0.1
94916 NCI-H292 Mucoepidermoid lung carcinoma sscDNA	2.3	1.5
94917 DMS-114 Small cell lung cancer sscDNA	0	0.1
94918 DMS-79 Small cell lung cancer/neuroendocrine sscDNA	0	0
94919 NCI-H146 Small cell lung cancer/neuroendocrine sscDNA	5.8	5.4
94920 NCI-H526 Small cell lung cancer/neuroendocrine sscDNA	0.3	0
94921 NCI-N417 Small cell lung cancer/neuroendocrine sscDNA	2.3	1.9
94923 NCI-H82 Small cell lung cancer/neuroendocrine sscDNA	0.5	0.3
94924 NCI-H157 Squamous cell lung cancer (metastasis) sscDNA	1.7	1.3
94925 NCI-H1155 Large cell lung cancer/neuroendocrine sscDNA	1.4	0.7
94926 NCI-H1299 Large cell lung cancer/neuroendocrine sscDNA	1.5	1.7
94927 NCI-H727 Lung carcinoid sscDNA	0	0
94928 NCI-UMC-11 Lung carcinoid sscDNA	26.4	21.9
94929 LX-1 Small cell lung cancer sscDNA	0	0
94930 Colo-205 Colon cancer sscDNA	0	0
94931 KM12 Colon cancer sscDNA	0	0
94932 KM20L2 Colon cancer sscDNA	0	0
94933 NCI-H716 Colon cancer sscDNA	0.6	0.5
94935 SW-48 Colon adenocarcinoma sscDNA	0	0
94936 SW1116 Colon adenocarcinoma sscDNA	0.1	0
94937 LS 174T Colon adenocarcinoma sscDNA	0	0
94938 SW-948 Colon adenocarcinoma sscDNA	0	0
94939 SW-480 Colon adenocarcinoma sscDNA	0	0
94940 NCI-SNU-5 Gastric carcinoma sscDNA	0	0
94941 KATO III Gastric carcinoma sscDNA	0.2	0
94943 NCI-SNU-16 Gastric carcinoma sscDNA	0.8	0.7
94944 NCI-SNU-1 Gastric carcinoma sscDNA	0	0
94946 RF-1 Gastric adenocarcinoma sscDNA	0.9	0.9
94947 RF-48 Gastric adenocarcinoma sscDNA	0.8	2
96778 MKN-45 Gastric carcinoma sscDNA	0	0
94949 NCI-N87 Gastric carcinoma sscDNA	0	0
94951 OVCAR-5 Ovarian carcinoma sscDNA	0.7	0.7
94952 RL95-2 Uterine carcinoma sscDNA	7.8	2.7
94953 HelaS3 Cervical adenocarcinoma sscDNA	0	0
94954 Ca Ski Cervical epidermoid carcinoma (metastasis) sscDNA	0.6	0.6
94955 ES-2 Ovarian clear cell carcinoma sscDNA	1.4	2
94957 Ramos/6h stim "; Stimulated with PMA/ionomycin 6h sscDNA	9.7	16
94958 Ramos/14h stim "; Stimulated with PMA/ionomycin 14h sscDNA	9	13.9
94962 MEG-01 Chronic myelogenous leukemia (megakaryoblast) sscDNA	9.6	12.6

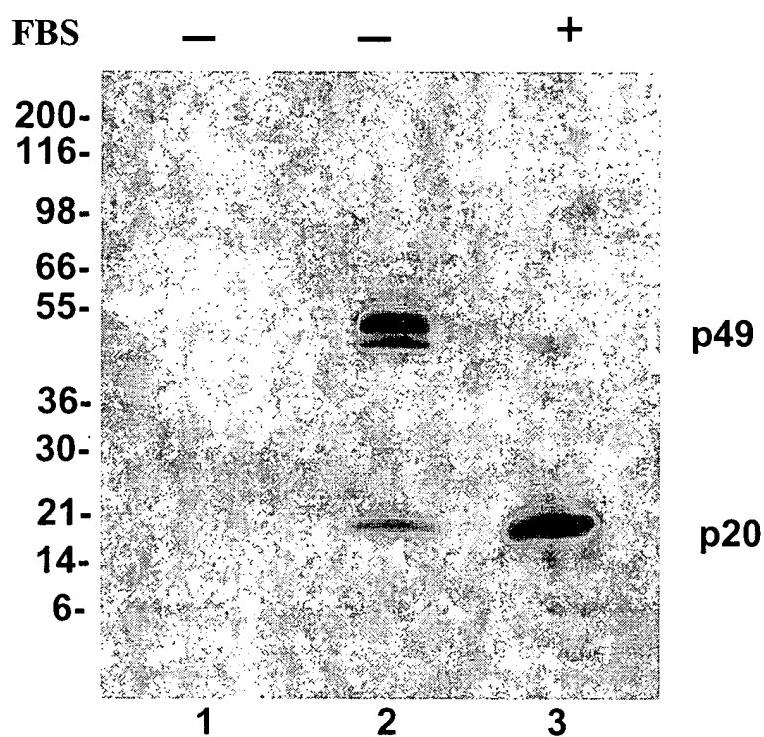
94963 Raji Burkitt's lymphoma sscDNA	3.6	4.1
94964 Daudi Burkitt's lymphoma sscDNA	6	9.1
94965 U266 B-cell plasmacytoma/myeloma sscDNA	0	0.2
94968 CA46 Burkitt's lymphoma sscDNA	0.8	1
94970 RL non-Hodgkin's B-cell lymphoma sscDNA	5.6	7.7
94972 JM1 pre-B-cell lymphoma/leukemia sscDNA	0.2	0.1
94973 Jurkat T cell leukemia sscDNA	0	0
94974 TF-1 Erythroleukemia sscDNA	5.6	5.3
94975 HUT 78 T-cell lymphoma sscDNA	0.1	0.2
94977 U937 Histiocytic lymphoma sscDNA	0	0
94980 KU-812 Myelogenous leukemia sscDNA	5.6	7.9
94981 769-P Clear cell renal carcinoma sscDNA	0.4	0.2
94983 Caki-2 Clear cell renal carcinoma sscDNA	4.8	4.8
94984 SW 839 Clear cell renal carcinoma sscDNA	0.4	1.2
94986 G401 Wilms' tumor sscDNA	1.4	1.4
94987 Hs766T Pancreatic carcinoma (LN metastasis) sscDNA	0	0.2
94988 CAPAN-1 Pancreatic adenocarcinoma (liver metastasis) sscDNA	0.3	0
94989 SU86.86 Pancreatic carcinoma (liver metastasis) sscDNA	2.5	1.7
94990 BxPC-3 Pancreatic adenocarcinoma sscDNA	0.1	0
94991 HPAC Pancreatic adenocarcinoma sscDNA	3.4	4.1
94992 MIA PaCa-2 Pancreatic carcinoma sscDNA	0	0
94993 CFPAC-1 Pancreatic ductal adenocarcinoma sscDNA	6.1	6.1
94994 PANC-1 Pancreatic epithelioid ductal carcinoma sscDNA	0.4	0
94996 T24 Bladder carcinoma (transitional cell) sscDNA	0.3	0.3
94997 5637 Bladder carcinoma sscDNA	1.3	0.7
94998 HT-1197 Bladder carcinoma sscDNA	2.6	1.1
94999 UM-UC-3 Bladder carcinoma (transitional cell) sscDNA	0	0
95000 A204 Rhabdomyosarcoma sscDNA	0	0
95001 HT-1080 Fibrosarcoma sscDNA	0	0
95002 MG-63 Osteosarcoma (bone) sscDNA	0.1	0.5
95003 SK-LMS-1 Leiomyosarcoma (vulva) sscDNA	0.2	0
95004 SJRH30 Rhabdomyosarcoma (met to bone marrow) sscDNA	5.1	5.7
95005 A431 Epidermoid carcinoma sscDNA	0	0
95007 WM266-4 Melanoma sscDNA	0.9	0.7
95010 DU 145 Prostate carcinoma (brain metastasis) sscDNA	0	0.2
95012 MDA-MB-468 Breast adenocarcinoma sscDNA	0	0
95013 SCC-4 Squamous cell carcinoma of tongue sscDNA	0	0
95014 SCC-9 Squamous cell carcinoma of tongue sscDNA	0	0
95015 SCC-15 Squamous cell carcinoma of tongue sscDNA	0	0
95017 CAL 27 Squamous cell carcinoma of tongue sscDNA	0	0

FIG. 14



Exhibit C

A



B

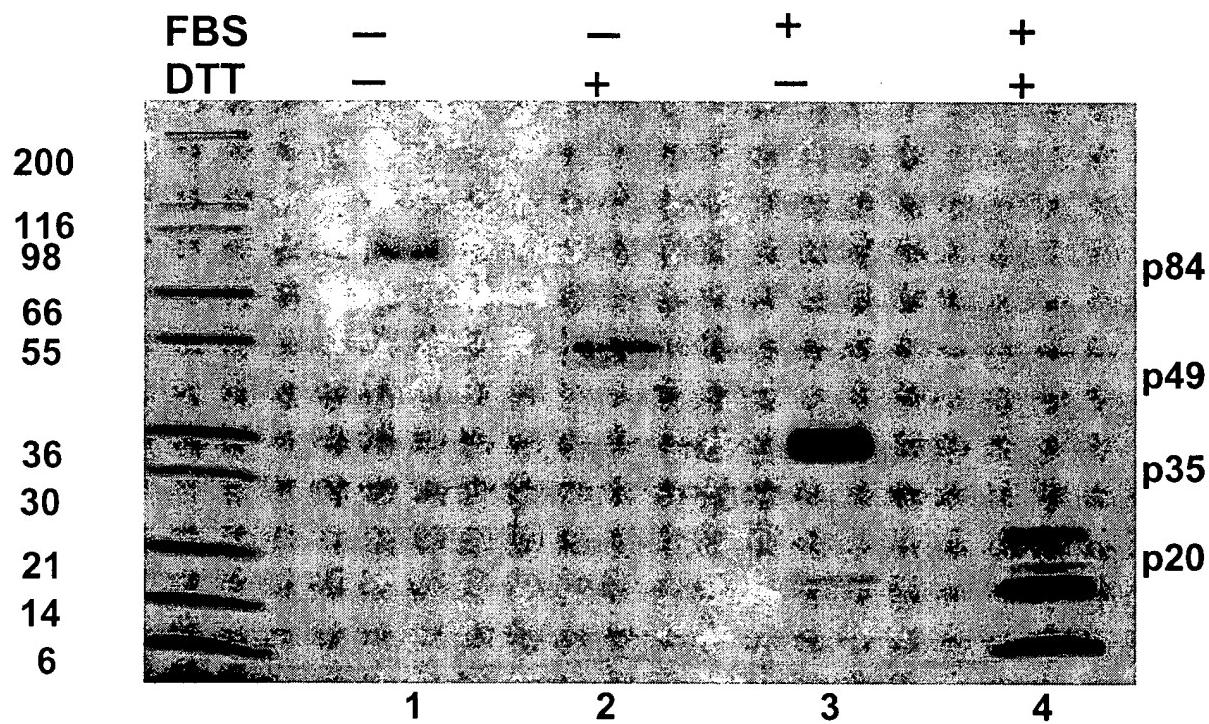
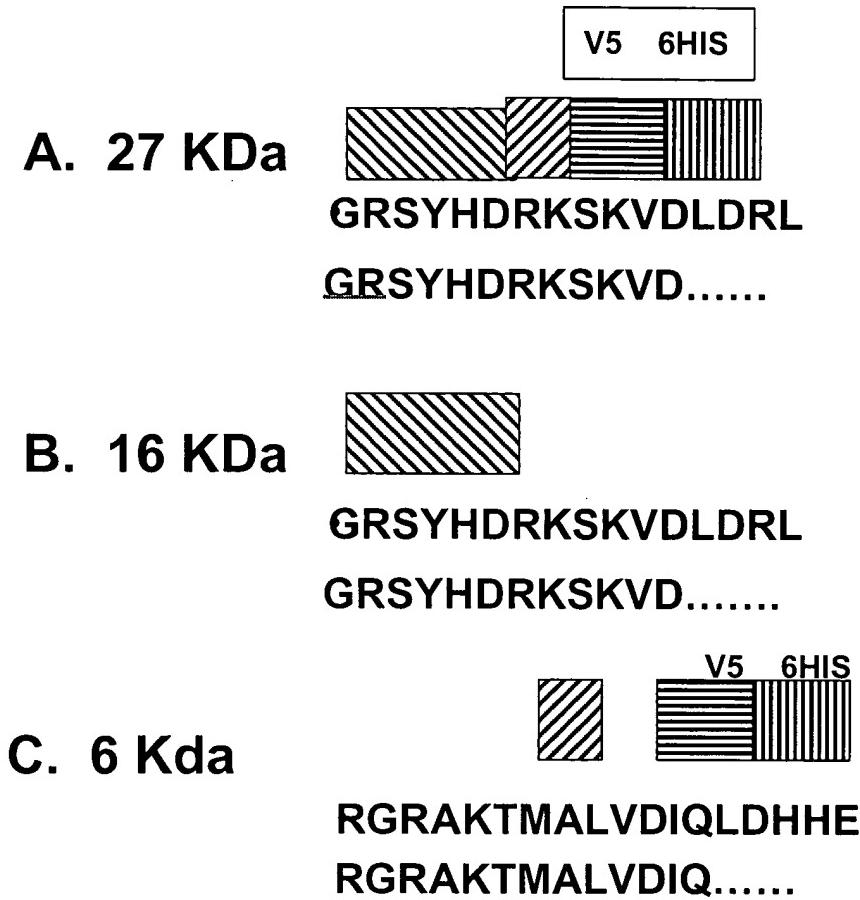


Exhibit C (cont.)

FIG. 15



TRA 1675833v2